IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Kirchholtes et al.

Serial No.: 09/787,215

Filed: May 17, 2001

For: HIGH PURITY COMPOSITION COMPRISING (7α, 17α)-17-HYDROXY-7-METHYL-19-NOR-17-PREGN-5(10)-EN-20-YN-3-ONE

Examiner: S. Jiang

Group Art Unit: 1617

Attorney Docket No.: D/98409 US
(5047US)

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RESPONSE

Box Non-Fee Amendment
Commissioner for Patents
Washington, D.C. 20231

Sir:

The Office Action mailed July 31, 2001, has been received and reviewed. Claims 1-18 are stated to be pending, however, claim 8 was previously cancelled in the Preliminary Amendment filed on March 15, 2001. Therefore, claims 1-7 and 9-18 are currently pending. All claims stand rejected. Reconsideration is respectfully requested.

1. 35 U.S.C. § 102

A. Claims 1-3, 7, and 9 - Sas

Claims 1-3, 7, and 9 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Sas et al. (EP 389035 A1) ("Sas"). Applicants respectfully traverse the rejection.

Applicants respectfully submit that the presently claimed invention is not anticipated by Sas. Independent claim 1 recites highly pure (7α, 17α)-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one comprising (7α, 17α)-17-hydroxy-7-methyl-19-nor-17-pregn-4-en-20-yn-3-one in an amount less than 0.5% by weight. Claims 2, 3, and 7 depend from claim 1. The inventors found that a small amount of (7α, 17α)-17-hydroxy-7-methyl-19-nor-17-pregn-4-en-20-yn-3-one is always found as an impurity in compositions of (7α, 17α)-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one because the impurity is more stable than the desired compound. The impurity forms by an acid catalyzed isomerization of (7α, 17α)-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one. In addition, the impurity forms at higher temperatures or during long term storage of formulations containing (7α, 17α)-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one.

In contrast, Sas discloses a pharmaceutical composition containing the compound (7α, 17α)-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one. This compound is polymorphous and forms in two crystalline pure forms, referred to as "Form 1" and "Form 2." While the two crystalline forms are structurally identical, they differ in their conformations. Specifically, the A ring of Form 1 is 2β,3α half chair while the A ring of Form 2 is 2α,3β half chair. Sas discloses that the composition is crystalline pure, which means that the composition of one crystalline form of (7α, 17α)-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one is completely free of the other crystalline form. Sas discloses a method of preparing both Form 1 and Form 2 of the compound using different crystallization conditions. However, Sas is silent about the presence of any impurities in the composition, such as (7α, 17α)-17-hydroxy-7-methyl-19-nor-17-pregn-4-en-20-yn-3-one.

Accordingly, applicants respectfully request that the rejection under 35 U.S.C. § 102(b) be withdrawn with respect to independent claim 1 and claims 2, 3, 7 which depend directly therefrom.

With respect to independent claim 9, it defines a dosage unit comprising a pharmaceutically suitable solid carrier and (7α, 17α)-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one in an amount of less than 2.50 mg, which is less than 5% by weight of (7α, 17α)-17-hydroxy-7-

methyl-19-nor-17-pregn-4-en-20-yn-3-one. Since Sas does not teach or suggest that (7α, 17α)-17-hydroxy-7-methyl-19-nor-17-pregn-4-en-20-yn-3-one is an impurity, applicants respectfully request that the rejection of claim 9 be withdrawn for the same reasons presented above.

B. Claims 9-18 - de Haan

Claims 9-18 stand rejected under 35 U.S.C. § 102(b) as being anticipated by de Haan et al. (WO 98/47517) ("de Haan"). Applicants respectfully traverse this rejection.

Applicants respectfully point out that de Haan is not prior art to the instant application. The publication date of de Haan is October 29, 1998, some 13 days after applicants' Paris Convention priority date.

As de Haan is not prior art to the instant application, applicants respectfully request that the rejection under 35 U.S.C. § 102(b) be withdrawn with respect to independent claim 9 and claims 10-18 which depend therefrom.

2. 35 U.S.C. § 103

A. Claims 4-6 - Sas and van Vliet

Claims 4-6 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Sas and van Vliet et al. (*Recueil des Travaux Chimiques des Pays-Bas*, April 1986, 105/4:111-115) ("van Vliet"). Applicants respectfully traverse this rejection, as hereinafter set forth.

Applicants respectfully submit that the claims are not rendered obvious by Sas. As discussed previously herein, Sas discloses a crystalline pure pharmaceutical composition of (7α, 17α)-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one, where the two forms of the polymorphous compound can be crystallized using different conditions. Sas does not disclose impurities in the composition.

Claims 4-6 depend directly and indirectly on claim 1 and include all the limitations of claim 1. Therefore, claims 4-6 include the limitation that the composition has (7α, 17α)-17-hydroxy-7-methyl-19-nor-17-pregn-4-en-20-yn-3-one in an amount less than 0.5% by weight.

In contrast with Sas, the presently claimed invention discloses highly pure (7α, 17α)-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one comprising the impurity (7α, 17α)-17-hydroxy-7-methyl-19-nor-17-pregn-4-en-20-yn-3-one in an amount less than 0.5% by weight. The

latter compound results from an acid catalyzed isomerization that occurs at higher temperatures and during long term storage. Since Sas does not disclose this impurity, Sas does not teach or suggest all the limitations of the claimed invention.

van Vliet fails to correct this deficiency of Sas. van Vliet discloses an alternative method of synthesizing (7α, 17α)-17-hydroxy-7-methyl-19-nor-17-pregn-5(10)-en-20-yn-3-one. While van Vliet discloses that (7α, 17α)-17-hydroxy-7-methyl-19-nor-17-pregn-4-en-20-yn-3-one (labeled as Compound 21) is a potential impurity in this synthesis, it only discloses that the impurity is present at less than 1%. *See,* van Vliet, p.113.

As the proposed combination of Sas and van Vliet fails to teach or suggest every element of the presently claimed invention, applicants respectfully submit that the presently claimed invention is not obvious over the combination of references. Reconsideration is respectfully requested.

Conclusion

In view of the remarks, applicants respectfully submit that the claims define patentable subject matter. If questions should remain after consideration of the foregoing, the Examiner is kindly requested to contact applicants' attorney at the address or telephone number given herein.

Respectfully submitted,

Katherine Hamer

Katherine Hamer
Registration No. 47,628
Attorney for Applicants
Trask, Britt PC
P. O. Box 2550
Salt Lake City, Utah 84110-2550
Telephone: (801) 532-1922

Date: October 31, 2001
N:\1963\5047\Response to office action rev.wpd

Attorney Docket No. [illegible]

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Examiner:	S. Jiang	Group Art Unit No.:	1617
Applicant(s):	Kirchholtes et al.	Filing date:	May 17, 2001
Serial No.:	09/787,215	For (title):	HIGH PURITY COMPOSITION COMPRISING (7α, 17α)-17-HYDROXY-7-METHYL-19-NOR-17-PREGN-5(10)-EN-20-YN-3-ONE

COMMUNICATION TRANSMITTAL

Commissioner for Patents
Washington, D.C. 20231

Sir:

Enclosed for filing in connection with the above-identified patent application, and submitted in the order listed, are:

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☒ Duplicate copy of this transmittal sheet in the event that additional filing fees are required under 37 C.F.R. § 1.16. Any such fees may be charged to deposit account no. 20-1469.
☐ Check no. in the amount of $ for the presentation of extra claims as calculated in the remarks section below.
☐ Preliminary amendment.
☒ Amendment or other communication in response to the non-final office action mailed July 31, 2001.
☐ Amendment or other communication under 37 C.F.R. § 1.116 in response to the final office action mailed .
☐ Petition for Extension of Time in duplicate with check no. in the amount of $.
☐ Verified statement(s) to establish small entity status under 37 C.F.R. § 1.9 and 37 C.F.R. § 1.27 signed by (or on behalf of) .
☐ Information disclosure statement and information disclosure citation form PTO-1449 with copies of listed documents.
☐

Remarks:

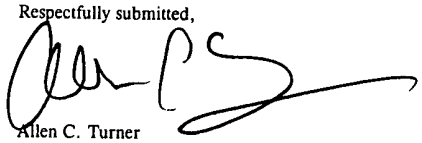
☐ An amendment has been made involving one or more claims in the application. The calculation to determine whether any additional fee is due is presented below.

	1		2		3		$EXTRA
Total claims		-		=		x $18.00 =	
Indep. claims		-		=		x $84.00 =	
First presentation of a multiple dep. claim (+$280.00)							
SUBTOTAL							
Reduction for small entity - 50% of subtotal*							
TOTAL ADDITIONAL FEE (subtotal minus any reduction)							

*Verified statement(s) must be attached to support this reduction if small entity status has not been previously established.
1 Claims remaining after amendment.
2 Highest number of claims previously paid for. Not less than 20 for total claims and 3 for independent claims.
3 Difference between claims remaining and highest number previously paid for. If less than zero, enter "0."

☒ The commissioner is authorized to charge any additional fees required but not submitted with any document or request requiring fee payment under 37 C.F.R. §§ 1.16 and 1.17 to deposit account no. 20-1469 during the entire pendency of this application.

Respectfully submitted,



Allen C. Turner
Reg. No. 33,041
TRASK BRITT
P.O. Box 2550
Salt Lake City, UT 84110-2550
(801) 532-1922

Date: October 31, 2001
Enclosures: As identified above